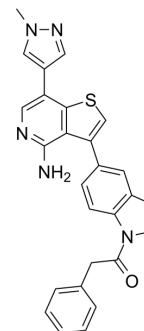


## GSK2593074A

|                           |   |       |          |
|---------------------------|---|-------|----------|
| <b>Cat. No.:</b>          | HY-122909   |       |          |
| <b>CAS No.:</b>           | 1337531-06-2                                      |       |          |
| <b>Molecular Formula:</b> | C <sub>27</sub> H <sub>23</sub> N <sub>5</sub> OS |       |          |
| <b>Molecular Weight:</b>  | 465.57  |       |          |
| <b>Target:</b>            | RIP kinase  |       |          |
| <b>Pathway:</b>           | Apoptosis   |       |          |
| <b>Storage:</b>           | Powder  | -20°C | 3 years  |
|                           |   | 4°C   | 2 years  |
|                           | In solvent  | -80°C | 6 months |
|                           |   | -20°C | 1 month  |



### SOLVENT & SOLUBILITY

|   |   |                          |            |            |
|---|---|--------------------------|------------|------------|
| <b>In Vitro</b>   | DMSO : 41.67 mg/mL (89.50 mM; Need ultrasonic)  |                          |            |            |
|   |   | Solvent<br>Concentration | Mass       |            |
|   |   |                          | 1 mg       | 5 mg       |
|   |   |                          | 10 mg      |            |
| <b>Preparing Stock Solutions</b>  | <b>1 mM</b>   | 2.1479 mL                | 10.7395 mL | 21.4790 mL |
|   | <b>5 mM</b>   | 0.4296 mL                | 2.1479 mL  | 4.2958 mL  |
|   | <b>10 mM</b>  | 0.2148 mL                | 1.0740 mL  | 2.1479 mL  |
| Please refer to the solubility information to select the appropriate solvent. |   |                          |            |            |
| <b>In Vivo</b>  | 1. Add each solvent one by one: 10% DMSO >> 40% PEG300 >> 5% Tween-80 >> 45% saline<br>Solubility: ≥ 2.08 mg/mL (4.47 mM); Clear solution |                          |            |            |

### BIOLOGICAL ACTIVITY

|                                     |  |
|-------------------------------------|--|
| <b>Description</b>                  | GSK2593074A (GSK'074) is a necroptosis inhibitor with dual targeting ability to both RIP1 and RIP3 <sup>[1]</sup> .  |
| <b>IC<sub>50</sub> &amp; Target</b> | RIP1, RIP3 <sup>[1]</sup>  |
| <b>In Vitro</b>                     | GSK2593074A (GSK'074; 0.01, 0.1, 1, 10, and 100 nM; 6 hours for MOVAS cells; 3 hours for L929 cells) completely rescues cells from necroptosis under different stimuli in both human and murine cells at IC <sub>50</sub> ~3 nM. In multiple cell types including mouse SMCs, fibroblasts (L929), bone marrow derived macrophages (BMDM), and human colon epithelial cells (HT29), GSK2593074A inhibits necroptosis with an IC <sub>50</sub> of ~3 nM <sup>[1]</sup> .<br>MCE has not independently confirmed the accuracy of these methods. They are for reference only.<br>Cell Viability Assay <sup>[1]</sup> |

|                  |   |               |  |                |                              |                  |   |         |   |
|------------------|---|---------------|--|----------------|------------------------------|------------------|---|---------|---|
|                  | <table border="1"> <tr> <td>Cell Line:</td> <td>Mouse smooth muscle cell line MOVAS; Mouse fibroblast cell line L929</td> </tr> <tr> <td>Concentration:</td> <td>0.01, 0.1, 1, 10, and 100 nM</td> </tr> <tr> <td>Incubation Time:</td> <td>6 hours for MOVAS cells; 3 hours for L929 cells</td> </tr> <tr> <td>Result:</td> <td>Inhibited MOVAS and L929 cells with the IC<sub>50</sub> of 3 nM.</td> </tr> </table>   | Cell Line:    | Mouse smooth muscle cell line MOVAS; Mouse fibroblast cell line L929 | Concentration: | 0.01, 0.1, 1, 10, and 100 nM | Incubation Time: | 6 hours for MOVAS cells; 3 hours for L929 cells | Result: | Inhibited MOVAS and L929 cells with the IC <sub>50</sub> of 3 nM. |
| Cell Line:       | Mouse smooth muscle cell line MOVAS; Mouse fibroblast cell line L929  |               |  |                |                              |                  |   |         |   |
| Concentration:   | 0.01, 0.1, 1, 10, and 100 nM  |               |  |                |                              |                  |   |         |   |
| Incubation Time: | 6 hours for MOVAS cells; 3 hours for L929 cells   |               |  |                |                              |                  |   |         |   |
| Result:          | Inhibited MOVAS and L929 cells with the IC <sub>50</sub> of 3 nM.   |               |  |                |                              |                  |   |         |   |
| <b>In Vivo</b>   | <p>GSK2593074A (GSK'074; 0.93 mg/kg/day; i.p. injection; 14 or 28 days) is administrated to Apoe<sup>-/-</sup> mice immediately following pump implantation. Compared to the DMSO group, GSK2593074A-treated mice show significantly alleviated aneurysm formation, reflected by a much smaller aortic dilatation (DMSO 85.39±15.76% vs GSK2593074A 36.28±5.76%; P&lt;0.05) as well as a reduced abdominal aortic aneurysm (AAA) incidence (from 83.3 to 16.7%). GSK2593074A significantly decreases the extent of aortic expansion (DMSO 66.06±9.17% vs GSK2593074A 27.36±8.25%; P&lt;0.05) [1].</p> <p>MCE has not independently confirmed the accuracy of these methods. They are for reference only.</p> <table border="1"> <tr> <td>Animal Model:</td> <td>Apoe<sup>-/-</sup> female mice (9-10 months)<sup>[1]</sup></td> </tr> <tr> <td>Dosage:</td> <td>0.93 mg/kg/day; 200 µL</td> </tr> <tr> <td>Administration:</td> <td>Daily i.p. injection; 14 or 28 days</td> </tr> <tr> <td>Result:</td> <td>Inhibited aneurysm formation in mouse models of aneurysms.</td> </tr> </table> | Animal Model: | Apoe <sup>-/-</sup> female mice (9-10 months) <sup>[1]</sup>         | Dosage:        | 0.93 mg/kg/day; 200 µL       | Administration:  | Daily i.p. injection; 14 or 28 days             | Result: | Inhibited aneurysm formation in mouse models of aneurysms.        |
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| Result:          | Inhibited aneurysm formation in mouse models of aneurysms.  |               |  |                |                              |                  |   |         |   |

## REFERENCES

[1]. Zhou T, et al. Identification of a novel class of RIP1/RIP3 dual inhibitors that impede cell death and inflammation in mouse abdominal aortic aneurysm models. Cell Death Dis. 2019 Mar 6;10(3):226.

**Caution: Product has not been fully validated for medical applications. For research use only.**

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